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For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

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In the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A compound of Formula I or Formula II

pharmaceutically acceptable salt thereof;

which has the property of inhibiting the activation of Met by HGF/SF in cancer cells at a concentration below 10⁻¹¹M, wherein

R¹ is <u>a</u> lower alkyl, <u>lower</u> alkenyl[[,]] <u>lower or</u> alkynyl[[,]]; <u>optionally a</u> substituted lower alkyl, alkenyl[[,]] or alkynyl; <u>a</u> lower alkoxy, alkenoxy <u>and or</u> alkynoxy; <u>a</u> straight or branched <u>alkylamines</u> <u>alkylamine</u>, alkenyl <u>amines and amine or</u> alkynyl <u>amines amine</u>; <u>or</u> a 3-6 member heterocyclic group that is optionally substituted;

R² is H, <u>a</u> lower alkyl, <u>lower</u> alkenyl[,]] <u>or lower</u> alkynyl, <u>optionally</u> <u>a</u> substituted lower alkyl, alkenyl[[,]] or allynyl; <u>a</u> lower alkoxy, alkenoxy <u>and or</u> alkynoxy; <u>a</u> straight <u>and or</u> branched <u>alkylamines</u> <u>alkylamine</u>, alkenyl <u>amines and amine or</u> alkynyl amines; <u>or</u> a 3-6 member heterocyclic group that is optionally substituted;

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R³ is H[[,]]; <u>a</u> lower alkyl, <u>lower</u> alkenyl[[,]] <u>or lower</u> alkynyl[[,]]; <u>optionally a</u> substituted lower alkyl, alkenyl[[,]] or alkynyl; <u>a</u> lower alkoxy, alkenoxy <u>and or</u> alkynoxy; <u>a</u> straight or branched <u>alkylamines</u> <u>alkylamine</u>, alkenyl <u>amines</u>[[,]] <u>amine or</u> alkynyl <u>amines</u> <u>amine</u>; or wherein the N is a member of a heterocycloalkyl, heterocylokenyl or heteroaryl ring that is optionally substituted;

R⁴ is H[[,]]; <u>a</u> lower alkyl, lower alkenyl[[,]] <u>or lower</u> alkynyl, optionally <u>a</u> substituted lower alkyl, alkenyl[[,]] or alkynyl, and wherein

the ring double bonds between positions $C_2=C_3$, $C_4=C_5$, and $C_8=C_9$ are optionally hydrogenated to single bonds.

- 2. (Original) The compound of claim 1 which is a benzoquinone compound of Formula I.
- 3. (Original) The compound of claim 1 which is a hydroquinone compound of Formula II.
- 4. (Original) The compound of claim 1 that inhibits the activation of Met by HGF/SF in cancer cells at a concentration below 10⁻¹³M.
- 5. (Original) The compound of claim 4 that inhibits the activation of Met by HGF/SF in cancer cells at a concentration below 10⁻¹⁵M.
- 6. (Original) The compound of claim 5 that inhibits the activation of Met by HGF/SF in cancer cells at a concentration below 10-¹⁷M.
- 7. (Currently Amended) The compound of any of claims [[1-6]] claim 1 wherein R¹ is a 3-6 member heterocyclic ring and wherein N is the heteroatom.
- 8. (Currently Amended) The compound of any of claims [[1-7]] claim 1 wherein each of R^2 , R^3 and R^4 is H.

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- 9. (Currently Amended) The compound of claim 1 selected from the group consisting of:
 - (a) 17-(2-Fluoroethyl)amino-17-demethoxygeldanamycin;
 - (b) 17-Allylamino-17-demethoxygeldanamycin;
 - (c) 17-N-Aziridinyl-17-demethoxygeldanamycin;
 - (d) 17-Amino-17-demethoxygeldanamycin;
 - (e) 17-N-Azetidinyl-17-demethoxygeldanamycin;
 - (f) 17-(2-Dimethylaminoethyl)amino-17-demethoxygeldanamycin;
 - (g) 17-(2-Chloroethyl)amino-17-demethoxygeldanamycin; and
 - (h) Dihydrogeldanamycin.
- 10. (Currently Amended) A pharmaceutical compositions comprising
 - (a) the compound of any of claims [[1-9]] claim 1; and
 - (b) a pharmaceutically acceptable carrier or excipient.
- 11. (Currently Amended) A method of inhibiting a HGF/SF-induced, Met receptor mediated biological activity of a Met-bearing tumor or cancer cell, comprising providing to said cells an effective amount of a compound according to any of claims [[1-9]] claim 1 which compound has an IC₅₀ of less than about 10⁻¹³M for inhibition of said biological activity.
- 12. (Original) The method of claim 11 wherein said biological activity is the induction of uPA activity in said cells.
- 13. (Original) The method of claim 11 wherein said biological activity is growth or scatter of said cells.
- 14. (Original) The method of claim 13 wherein said growth of said cells is in vitro.
- 15. (Original) The method of claim 13 wherein said growth of said cells is in vivo.

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16. (Original) The method of claim 11 wherein said biological activity is invasion of said

cells.

17. (Original) The method of claim 16 wherein said invasion is in vitro.

18. (Original) The method of claim 16 wherein said invasion is in vivo.

19. (Original) The method of claim 16 wherein said invasion results in tumor metastasis.

20. (Currently Amended) A method of inhibiting in a subject metastasis of Met-bearing tumor or cancer cells that is induced by HGF/SF, comprising providing to said subject an effective amount of a compound according to any of claims [[1-9]] claim 1, which compound

has an IC50 of less than about 10⁻¹²M for inhibition tumor cell invasion when measured in an

assay in vitro.

21. (Original) A method of inhibiting in a subject metastasis of Met-bearing tumor or cancer cells that is induced by HGF/SF, comprising providing to said subject an effective amount of a pharmaceutical composition according to claim 10 which composition comprises a chemical compound that has an IC50 of less than about 10⁻¹²M for inhibition tumor cell invasion

when measured in an assay in vitro.

22. (Currently Amended) The method of any of claims [[11-19]] claim 11 wherein said inhibition results in measurable regression of a tumor caused by said cells or measurable

attenuation of tumor growth in said subject.

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23. (Currently Amendedl) A method of protecting against growth or metastasis of a Metpositive tumor in a susceptible subject, comprising administering to said subject who is either

- (a) at risk for development of said tumor, or
- (b) in the case of an already treated subject, at risk for recurrence of said tumor, an effective amount of the compound of any of claims [[1-9]] claim 1 or the pharmaceutical composition of claim [[10]].
- 24. (Original) The method of claim 23 wherein the subject is a human.
- 25. (Currently Amended) A method of inducing an antitumor or anticancer response in a mammal having an HGF-responsive Met-expressing tumor, comprising administering an effective amount of the compound of any of claims [[1-9]] claim 1 or a pharmaceutical composition of claim [[10]] to said mammal, thereby inducing an antitumor or anticancer response which is
 - (a) a partial response characterized by
 - (i) at least a 50% decrease in the sum of the products of maximal perpendicular diameters of all measurable lesions;
 - (ii) no evidence of new lesions, and
 - (iii) no progression of any preexisting lesions, or
 - (b) a complete response characterized by the disappearance of all evidence of tumor or cancer disease for at least one month.
- 26. (Original) The method of claim 25 wherein said antitumor or anticancer response is a partial antitumor or anticancer response.
- 27. (Currently Amended) The method of claim 25 Θ [[26]] wherein the mammal is a human.

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28. (Currently Amended) A compound according to any of claims [[1-9]] claim 1 which is detectably labeled with a halogen radionuclide.

- 29. (Original) The compound of claim 28 wherein the radionuclide is bonded to the R¹ group.
- 30. (Currently Amended) The compound of claim 28 or [[29]] wherein the radionuclide is selected from the group consisting of ¹⁸F, ⁷⁶Br, ¹²³I, ¹²⁴I, and ¹³¹I.
- 31. (Currently Amended) A method of imaging a tumor in a subject which is a target of a composition of any of claims [[1-9,]] comprising administering an effective amount of a labeled compound according to any of claims [[28-30]] claim 28, and imaging the detectable label with an imaging means.